



INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

<p>(51) International Patent Classification ⁶ : C07H 21/00, A61K 31/70</p>	A3	<p>(11) International Publication Number: WO 98/55495</p> <p>(43) International Publication Date: 10 December 1998 (10.12.98)</p>																																	
<table style="width: 100%; border: none;"> <tr> <td style="width: 50%; vertical-align: top; padding: 5px;"> <p>(21) International Application Number: PCT/US98/11578</p> <p>(22) International Filing Date: 5 June 1998 (05.06.98)</p> <p>(30) Priority Data: 60/048,793 6 June 1997 (06.06.97) US</p> <p>(71) Applicant (for all designated States except US): DYNAVAX TECHNOLOGIES CORPORATION [US/US]; Suite 500, 3099 Science Park Road, San Diego, CA 92121 (US).</p> <p>(72) Inventors; and (75) Inventors/Applicants (for US only): SCHWARTZ, David [US/US]; 1544 Valleda Lane, Encinitas, CA 92024 (US). ROMAN, Mark [US/US]; 8742-33 Villa La Jolla Drive, La Jolla, CA 92037 (US). DINA, Dino [US/US]; 6140 Buena Vista Avenue, Oakland, CA 94618 (US).</p> <p>(74) Agents: LEHNHARDT, Susan, K. et al.; Morrison & Foerster LLP, 755 Page Mill Road, Palo Alto, CA 94304-1018 (US).</p> </td> <td style="width: 50%; vertical-align: top; padding: 5px;"> <p>(81) Designated States: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, ARIPO patent (GH, GM, KE, LS, MW, SD, SZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG).</p> <p>Published <i>With international search report.</i> <i>Before the expiration of the time limit for amending the claims and to be republished in the event of the receipt of amendments.</i></p> <p>(88) Date of publication of the international search report: 27 May 1999 (27.05.99)</p> </td> </tr> </table>			<p>(21) International Application Number: PCT/US98/11578</p> <p>(22) International Filing Date: 5 June 1998 (05.06.98)</p> <p>(30) Priority Data: 60/048,793 6 June 1997 (06.06.97) US</p> <p>(71) Applicant (for all designated States except US): DYNAVAX TECHNOLOGIES CORPORATION [US/US]; Suite 500, 3099 Science Park Road, San Diego, CA 92121 (US).</p> <p>(72) Inventors; and (75) Inventors/Applicants (for US only): SCHWARTZ, David [US/US]; 1544 Valleda Lane, Encinitas, CA 92024 (US). ROMAN, Mark [US/US]; 8742-33 Villa La Jolla Drive, La Jolla, CA 92037 (US). DINA, Dino [US/US]; 6140 Buena Vista Avenue, Oakland, CA 94618 (US).</p> <p>(74) Agents: LEHNHARDT, Susan, K. et al.; Morrison & Foerster LLP, 755 Page Mill Road, Palo Alto, CA 94304-1018 (US).</p>	<p>(81) Designated States: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, ARIPO patent (GH, GM, KE, LS, MW, SD, SZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG).</p> <p>Published <i>With international search report.</i> <i>Before the expiration of the time limit for amending the claims and to be republished in the event of the receipt of amendments.</i></p> <p>(88) Date of publication of the international search report: 27 May 1999 (27.05.99)</p>																															
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<p>(54) Title: IMMUNOSTIMULATORY OLIGONUCLEOTIDES, COMPOSITIONS THEREOF AND METHODS OF USE THEREOF</p>																																			
<p>IL6 48h</p> <table border="1" style="margin: 10px auto; border-collapse: collapse;"> <caption>Approximate IL6 levels (ng/mL) at 48h</caption> <thead> <tr> <th>Oligo#</th> <th>10 µg/ml (hatched)</th> <th>1 µg/ml (solid)</th> </tr> </thead> <tbody> <tr><td>1</td><td>32</td><td>11</td></tr> <tr><td>2</td><td>24</td><td>11</td></tr> <tr><td>3</td><td>5</td><td>2</td></tr> <tr><td>4</td><td>18</td><td>6</td></tr> <tr><td>5</td><td>9</td><td>4</td></tr> <tr><td>6</td><td>15</td><td>7</td></tr> <tr><td>7</td><td>36</td><td>26</td></tr> <tr><td>8</td><td>6</td><td>2</td></tr> <tr><td>9</td><td>7</td><td>2</td></tr> <tr><td>10</td><td>5</td><td>2</td></tr> </tbody> </table>			Oligo#	10 µg/ml (hatched)	1 µg/ml (solid)	1	32	11	2	24	11	3	5	2	4	18	6	5	9	4	6	15	7	7	36	26	8	6	2	9	7	2	10	5	2
Oligo#	10 µg/ml (hatched)	1 µg/ml (solid)																																	
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3	5	2																																	
4	18	6																																	
5	9	4																																	
6	15	7																																	
7	36	26																																	
8	6	2																																	
9	7	2																																	
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<p>(57) Abstract</p> <p>The invention relates to immunostimulatory oligonucleotide compositions. These oligonucleotides comprise an immunostimulatory octanucleotide sequence. These oligonucleotides can be administered in conjunction with an immunostimulatory peptide or antigen. Methods for modulating an immune response upon administration of the oligonucleotide are also disclosed. In addition, an in vitro screening method to identify oligonucleotides with immunostimulatory activity is provided.</p>																																			

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EE	Estonia	LR	Liberia	SG	Singapore		

INTERNATIONAL SEARCH REPORT

national Application No

PCT/US 98/11578

A. CLASSIFICATION OF SUBJECT MATTER

IPC 6 C07H21/00 A61K31/70

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 6 C07H A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	KRIEG A M ET AL: "CPG MOTIFS IN BACTERIAL DNA TRIGGER DIRECT B-CELL ACTIVATION" NATURE, vol. 374, 6 April 1995, pages 546-549, XP000197060	1, 56, 60-63
A	see page 548, column 1; table 2	2, 3, 10, 11, 16, 17, 67, 68
X	SATO Y ET AL: "IMMUNOSTIMULATORY DNA SEQUENCES NECESSARY FOR EFFECTIVE INTRADERMAL GENE IMMUNIZATION" SCIENCE, vol. 273, 19 July 1996, pages 352-354, XP002058357 see abstract; page 354, note 13, first sequence	1, 3, 4, 56
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Further documents are listed in the continuation of box C.



Patent family members are listed in annex.

* Special categories of cited documents:

"A" document defining the general state of the art which is not considered to be of particular relevance

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"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

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"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"A" document member of the same patent family

Date of the actual completion of the international search

24 March 1999

Date of mailing of the international search report

06/04/1999

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Scott, J

INTERNATIONAL SEARCH REPORT

International Application No
PCT/US 98/11578

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT		
Category	Citation of document, with indication where appropriate, of the relevant passages	Relevant to claim No.
A	WO 95 26204 A (ISIS PHARMACEUTICALS INC) 5 October 1995 see the whole document ---	1,56
A	WO 96 02555 A (UNIV IOWA RES FOUND) 1 February 1996 see page 15, table 1, compounds 4-4h; page 21, line 10 - page 24, line 20 ---	1,56
A	BALLAS Z K ET AL: "INDUCTION OF NK ACTIVITY IN MURINE AND HUMAN CELLS BY CPG MOTIFS IN OLIGODEOXYNUCLEOTIDES AND BACTERIAL DNA" JOURNAL OF IMMUNOLOGY, vol. 157, September 1996, pages 1840-1845, XP002058359 see the whole document ---	1,56
P,X	WO 98 16247 A (CARSON DENNIS A ;RAZ EYAL (US); ROMAN MARK (US); UNIV CALIFORNIA () 23 April 1998 see page 37, lines 9,10, sequence DY1018; examples 2-4, claims 1,2,27,29,54,57,66; page 3, line 2 - page 4, line 11 ---	1,3-5, 25-32, 45-66
P,X	WO 98 18810 A (UNIV IOWA RES FOUND ;KLINE JOEL N (US); KRIEG ARTHUR M (US)) 7 May 1998 see the whole document, but especially, claim 1, claim 18, claim 23, sequence 2 ---	1,2,4, 45,46, 56,59,60
T	NGUYEN H ET AL: "Studies Towards the Design of a Modified GC Base Pair With Stability Similar to that of the AT Base Pair" TETRAHEDRON LETTERS, vol. 38, no. 23, 9 June 1997, page 4083-4086 XP004065032 see the whole document, and especially parts detailing 5-bromo-cytidine ---	1,2, 10-21
P,A	GRAYSON B LIPFORD ET AL: "Immunostimulatory DNA: sequence-dependent production of potentially harmful or useful cytokines" EUROPEAN JOURNAL OF IMMUNOLOGY, vol. 12, no. 27, December 1997, page 3420 3420 XP002077483 see the whole document -----	1,56

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US 98/11578

Box I Observations where certain claims were found unsearchable (Continuation of Item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☒ Claims Nos.: 45-70
because they relate to subject matter not required to be searched by this Authority, namely:
Remark: Although claims 45-70
are directed to a method of treatment of the human/animal
body, the search has been carried out and based on the alleged
effects of the compound/composition.
2. ☐ Claims Nos.:
because they relate to parts of the International Application that do not comply with the prescribed requirements to such
an extent that no meaningful International Search can be carried out, specifically:
3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of Item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all
searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment
of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report
covers only those claims for which fees were paid, specifically claims Nos.:
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is
restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

Information on patent family members

national Application No

PCT/US 98/11578

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 9526204 A	05-10-1995	US 5663153 A US 5723335 A	02-09-1997 03-03-1998
WO 9602555 A	01-02-1996	AU 1912795 A CA 2194761 A EP 0772619 A JP 10506265 T	16-02-1996 01-02-1996 14-05-1997 23-06-1998
WO 9816247 A	23-04-1998	AU 4992197 A	11-05-1998
WO 9818810 A	07-05-1998	AU 5242498 A	22-05-1998